S/N 10/522,045 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Okamoto et al.	Examiner:	Amanda Shaw
Serial No.:	10/522,045	Group Art Unit:	1634
Filed:	January 19, 2005	Docket No.:	10873.1576USWO
Title:	MICROORGANISM OR CELL COLLECTION METHOD, AND MICROORGANISM OR CELL COLLECTING IMPLEMENT USED FOR THE METHOD		

CERTIFICATE UNDER 37 CFR 1.6:
The undersigned hereby certifies that this correspondence is being sent via facsimile to the United States Patent & Trademark Office, Commissioner for Patents (MAIL STOP: APPEAL BRIEF-PATENTS) on May 19, 2009.

By: Justine Suleski
Name: Justine Suleski

Mail Stop: **Appeal Brief-Patents**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' BRIEF ON APPEAL

Dear Sir:

This Brief is presented in support of the Notice of Appeal filed March 31, 2009, from the final rejection of Claims 1, 4-12 and 14-26 of the above-identified application, as set forth in the Office Action mailed December 1, 2008 and maintained in the Advisory Action mailed March 25, 2009.

Please charge our Deposit Account No. 50-3478 in the amount of $540.00 to cover the required fee for filing this Brief.

I. REAL PARTY IN INTEREST

The application pending for this appeal has been assigned to ARKRAY, Inc., of Kyoto, Japan.

II. RELATED APPEALS AND INTERFERENCES

The Assignee, the Assignee's legal representatives, and the Appellants are unaware of any other appeals or interferences that will affect, be directly affected by or have a bearing on the Board's decision in this Appeal.

III. STATUS OF CLAIMS

Claims 2-3 and 13 are canceled. Claims 1, 4-12 and 14-26 are pending. Claims 1, 4-12 and 14-26 are the subject of this Appeal. Appendix A attached herewith provides a copy of the claims in this Appeal.

IV. STATUS OF AMENDMENTS

A Response to the final Office Action was filed on March 2, 2009, under 37 C.F.R. § 1.116. By way of Advisory Action mailed March 25, 2009, the Response was considered, but deemed as not placing the application in condition for allowance.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 1, the sole independent claim in this application, is directed to a method of collecting a microorganism or a cell from a liquid sample. The method of claim 1 requires the use of a centrifugation tube 1 (see page 5, lines 17-18 of the specification and Fig. 1). The method requires the centrifugation tube 1 to comprise a planar filter 14 supported so as to divide the centrifugation tube 1 into an upper space and a lower space and water-absorbing resin particles 15 disposed on the filter 14 (see page 5, line 28 to page 6, line 2 of the specification and Fig. 1).

The method requires pouring the liquid sample into the centrifugation tube to bring the liquid sample into contact with the water-absorbing resin particles so that substantially all of a liquid phase part of the liquid sample is absorbed by the water-absorbing resin particles and the microorganism or the cell is caught on a surface of the water-absorbing resin particles (see page 6, lines 14-20 of the specification).

The method further requires pouring a collecting solution into the centrifugation tube to bring the collecting solution into contact with the water-absorbing resin particles, so as to collect

the microorganism or the cell caught on the surface of the water-absorbing resin particles in the collecting solution (see page 6, lines 23-29 of the specification). The method requires the collecting solution to be poured into the centrifugation tube without separating the liquid phase part absorbed by the water-absorbing resin particles from the water-absorbing resin particles that have absorbed the liquid phase part (see page 6, lines 16-29 of the specification).

The method also requires centrifuging the centrifugation tube so that the collecting solution containing the microorganism or the cell (i) separates from the water-absorbing resin particles by passing through the filter and (ii) accumulates at a bottom of the centrifugation tube (see page 7, lines 1-5 of the specification and Fig. 2D)

The advantageous effects of the method are explained as follows. In conventional methods of collecting microorganisms or cells such as TB bacteria, the bacteria is usually isolated, and then prepared separately for analysis such as PCR (see page 1, lines 18-27 of the specification). In such collection methods, the sample solution is first pre-treated to reduce the viscosity of the solution and then centrifuged so that the precipitated TB bacteria can be collected (see page 1, lines 27-34 of the specification). In these methods, the conditions for performing the centrifugation are severe, the operation for performing the centrifugation is complicated, and the centrifugation times are long (see page 1, line 34 to page 2, line 1 of the specification). These problems can be very significant, especially in situations where analysis of a large amount of sample is desired such as rivers, lakes or seas (see page 2, lines 23-26 of the specification). Moreover, in conventional methods, the isolated bacteria are then separately treated with a special device and/or special reagent so that sufficient gene extraction can be achieved (see page 2, lines 1-16 of the specification). Such additional steps can also increase the chances of introducing foreign contaminants that can impact significantly amplification results.

In contrast, the method of the present claims permit a quick shift from collection to a subsequent operation such as gene amplification, thereby shortening the time required for collection and preparation for PCR analysis to about 1/5 as compared to conventional methods, without using any special devices or special reagents (see page 11, line 35 to page 12, line 10 of the specification). Consequently, the method according to the present claims achieves a more efficient process for genetic analysis of a sample and at the same time, decreases the chances of

possible contamination as compared to conventional methods. These advantages are especially useful when the sample size is large, e.g., rivers, lakes, seas etc.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following issues are raised in the final rejection:

1. Whether claims 1, 4-12 and 14-26 are definite under 35 U.S.C. § 112, second paragraph;
2. Whether claims 1, 4-8, 10-12, 14 and 25-26 are obvious over Sato (US Publication No. 2001/0009759) in view of Wardlaw (US Publication No. 2001/0033808) in view of Lyman (US Patent No. 4683058) and Tsuchiya (US Patent No. 5747277);
3. Whether claims 9 and 16-24 are obvious over Sato in view of Lyman and Tsuchiya as applied to claims 1, 8 and 14 and in further view of US Patent No. 5,726,021 (Britschgi et al.). For purposes of this appeal alone, Appellants are not contesting the relevance of Britschgi et al. to claims 9 and 16-24 nor its suitability for combination with the remaining references. Claims 9 and 16-24 stand or fall with claim 1 from which claims 9 and 16-24 depend, and Britschgi et al. will not be addressed further in this Brief; and
4. Whether claim 15 is obvious over Sato in view of Lyman and Tsuchiya as applied to claim 14 and further in view of US Patent No. 5,658,779 (Krupey). For purposes of this appeal alone, Appellants are not contesting the relevance of Krupey to claim 15 nor its suitability for combination with the remaining references. Claim 15 stands or falls with claim 1 from which claim 15 depends, and Krupey will not be addressed further in this Brief.

VII. ARGUMENT

A. Claims 1, 4-12 and 14-26 are definite

Claims 1, 4-12 and 14-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. The rejection in particular contends that it is unclear if there is actually a liquid phase in the centrifugation tube prior to adding the collection solution.

Claim 1 recites pouring the liquid sample into the centrifugation tube so that substantially all of the liquid phase part of the liquid sample is absorbed by the water-absorbing particles, the water-absorbing particles being included within the centrifugation tube. Claim 1 further recites that the collecting solution is poured into the centrifugation tube without separating "the liquid phase part absorbed by the water absorbing resin particles" from the water absorbing resin particles that have absorbed the liquid phase part of the liquid sample. Thus, it is clear from the recited features that at the time the collecting solution is poured, the centrifugation tube includes the liquid phase part absorbed by the water-absorbing particles and the microorganism or cell caught on the surface of the water-absorbing resin particles. Thus, Applicants submit that claim 1 is fully consistent and definite.

Reversal of the rejection is respectfully requested.

B. Claims 1, 4-8, 10-12, 14 and 25-26 are patentable over Sato (US Publication No. 2001/0009759) in view of Wardlaw (US Publication No. 2001/0033808) in view of Lyman (US Patent No. 4683058) and Tsuchiya (US Patent No. 5747277)

Claims 1, 4-8, 10-12, 14 and 25-26 were rejected under 35 U.S.C. 103(a) as being unpatentable over Sato (US Publication No. 2001/0009759) in view of Wardlaw (US Publication No. 2001/0033808) in view of Lyman (US Patent No. 4683058) and Tsuchiya (US Patent No. 5747277). Appellants respectfully contend that the interpretation of the references is unreasonable for the following reasons.

Sato is directed to a method involving the use of particular type of particles for the specific purposes of isolating viruses in a sample in preparation for nucleic amplification (paragraph [0004]). Sato in particular stresses the importance of separating the viruses from other components in a sample due to the sensitivity of PCR (paragraph [0006] and [0167]).

For example, the reference notes that the prior art teaches soluble polymeric substances having cationic groups to separate viruses by sedimentation, and indicates that because the viruses are purified after sedimentation, the large quantity of protein mixed together with the viruses and the reagents to be mixed can inhibit the amplification of the viral gene (paragraph [0006]).

Sato teaches that their particles address this issue specifically by binding and thereby separating only the viruses for the purposes of examining and diagnosing the viruses using nucleic-acid amplification (paragraph [0007]). Sato teaches that the feature that permits specific binding of the viruses is the presence of at least one of a cationic and an anionic group on the surfaces of their particles (paragraph [0020], [0023] and [0065]).

Sato teaches that the cationic or the anionic group must be present in certain amounts; otherwise the particles may not possess virus-separating ability (paragraphs [0023] and [0065]). Sato indicates that the particles used can be hydrogel particles, but is silent as to the amounts of initiator or cross-linkers that can be used, which can impact significantly the liquid absorbing properties of hydrogels (paragraph [0074]).

Notably, Sato teaches that in their method, the particles are added to a sample in the form of a reagent prepared in an aqueous dispersion (paragraphs [0089] and [0097]). It can be understood from this description that Sato contemplates the use of particles in a dispersed state within an aqueous medium to allow the viruses to bind to the cationic or the anionic group on the surfaces of the particles within the mixture. Once the particles bind the viruses, the particles are removed from the liquid, e.g., by the use of magnets, and the viruses are then separated from the particles using a salt solution (paragraphs [0098-0099]). Thus, it can be further understood that if Sato's particles absorbed substantially all of the liquid part of the sample, the particles would no longer be in a dispersed state within an aqueous medium as intended by Sato, and as such, one would question whether the particles would bind effectively the viruses, and whether the virus-bound particles could be separated from the other components.

From the above, it is clear nothing in Sato teaches or suggests adding the sample into the virus-separating agent so that substantially all of the liquid part of the sample is absorbed by the virus-binding particles. It is also clear that nothing in Sato teaches or suggests adding a collecting solution without separating the liquid phase part of the sample absorbed by the virus-bound particles from the particles that have absorbed the liquid phase part of the sample.

Wardlaw is directed to separating components such as bacteria and cells from a liquid phase of a sample (paragraphs [0001] and [0012]). Wardlaw notes that the prior art teaches the separation of such constituents by the use of centrifugation and filtration, and that such methods can destroy the sample components or require prior knowledge as to the size of the target formed

constituents (paragraphs [0006-0007]). In order to address such issues, the reference teaches a technique that operates in a quiescent manner and does not require the use of centrifugation or filters (paragraph [0009]). In particular, the reference teaches the use of hydrogels to absorb substantially all of the liquid in a sample and thereby capture bacteria and cells on the planar surface of the hydrogel (paragraph [0012]).

It can be clearly understood from the above discussion that Wardlaw teaches that when a hydrogel absorbs substantially all of the liquid phase from a sample containing bacteria and cells, the bacteria and cells are drawn towards and captured on the surface of the hydrogel.

The rejection contends that Sato teaches a method of bringing a liquid sample into contact with the particles that in one embodiment are hydrogel particles which absorb water, that Wardlaw teaches absorbing resin particles that absorb substantially all of the liquid phase of the sample, that using hydrogel particles capable of absorbing essentially all of the liquid in the sample would aid in the separation and purification of the virus from the sample, and that it would have obvious to have modified Sato by using enough hydrogel particles to absorb essentially all of the liquid in the sample as suggested by Wardlaw.

However, as is clear from the discussion above, Sato is directed to achieving a result that is completely different from that of Wardlaw. That is, Sato is directed to separating the viruses from other components such as protein to enhance sensitivity of the amplification, whereas Wardlaw is directed to separating formed constituents in general for the purposes of viewing the separated components with an optical instrument. The use of hydrogel particles in amounts that would absorb essentially all of the liquid in the sample as taught by Wardlaw would in fact frustrate the purposes of Sato, as such use of the hydrogel particles would capture unwanted components that may adversely affect the amplification reaction of the viral gene, which is often very sensitive to the presence of other components as indicated by Sato.

The rejection contends that the Applicants have not provided any evidence that the particles would adsorb unwanted components. However, the teachings in Wardlaw provides a sufficient basis to conclude that if Sato's hydrogel is added in the same manner as that of Wardlaw, then components other than viruses such as bacteria and cells would be indiscriminately drawn towards and captured on the surface of the hydrogel.

Moreover, as indicated above, Sato teaches adding the virus-binding particles in the form

of an aqueous dispersion. Thus, it is clear that more of the hydrogel particles would need to be added in order to absorb essentially all of the liquid of the sample in addition to the liquid from the virus-separating reagent. The reference clearly notes that the addition of virus-binding particles in too large a quantity would be undesirable (paragraph [0097]). As such, it is far from clear whether the viruses would even separate if Sato's hydrogel particles were added in amounts that absorb essentially all of the liquid of the sample as indicated by the rejection.

The rejection contends that Sato merely states that in situations where there are small amounts of virus, the use of too many particles results in low separation. However, Sato clearly indicates in paragraph [0097] that the amount of the particles is dependent upon the amount of viruses present in the sample, and as discussed above, it is clear that more of the hydrogel particles would need to be added than the amount contemplated by Sato as being the proper amount, to absorb substantially all of the liquid in the reagent and the sample. Thus, one would in fact question whether the excess amount needed would allow proper separation of the viruses from the particles, as implicated by Sato.

The rejection further contends that it would have been obvious to have modified the method of Sato and Wardlaw by performing the step of binding the virus to the particles on a filter in a centrifuge and then centrifuging the tube so that the virus accumulates at the bottom of the centrifugation tube as suggested by Lyman and Tsuchiya. However, as indicated above, Sato specifically teaches that their particles capture only the viruses, and leads away from using the particles in a manner that would capture components other than viruses as taught by Wardlaw. As such, the combination of Sato and Wardlaw would frustrate the purposes of Sato. In addition, it can be clearly understood from Wardlaw as a whole that Wardlaw leads away from the use of centrifugation and filters as taught by Lyman and Tsuchiya. Thus, Applicants respectfully submit that it would not have been obvious to combine the references as indicated by the rejection.

Accordingly, for at least the above reasons, claim 1 is patentable over Sato, Wardlaw, Lyman and Tsuchiya, taken alone or together. Claims 4-12 and 14-26 are also patentable over the references since they depend from claim 1 that is allowable. Reversal of the rejection is respectfully requested.

C. Claims 9 and 16-24 are Allowable with Claim 1

Claims 9 and 16-24 are included in the rejection for obviousness over Sato in view of Lyman and Tsuchiya and further in view of Britschgi. As noted above in Section VI, for purpose of this appeal only, Appellants are not contesting the relevance of Britschgi to claims 9 and 16-24 nor its suitability for combination with Sato, Lyman and Tsuchiya. Claims 9 and 16-24 are allowable for at least the reasons discussed above for its independent claim 1.

D. Claim 15 is Allowable with Claim 1

Claim 15 is included in the rejection for obviousness over Sato in view of Lyman and Tsuchiya and further in view of Krupey. As noted above in Section VI, for purpose of this appeal only, Appellants are not contesting the relevance of Krupey to claim 15 nor its suitability for combination with Sato, Lyman and Tsuchiya. Claim 15 is allowable for at least the reasons discussed above for its independent claim 1.

VIII. CONCLUSION

Appellants submit that the rejections of claims 1, 4-12 and 14-26 are untenable for the reasons set forth above and should be reversed.

Please charge any additional fees or credit any overpayment to Hamre, Schumann, Mueller & Larson Deposit Account No. 50-3478.

Respectfully submitted,

Hamre, Schumann, Mueller & Larson, P.C.
P.O. Box 2902
Minneapolis, MN 55402-0902
Phone: 612-455-3800

Date: May 19, 2009

By _____
Name: Douglas P. Mueller
Reg. No. 30,300

APPENDIX A - PENDING CLAIMS

1. (rejected) A method of collecting a microorganism or a cell from a liquid sample, comprising:

pouring the liquid sample into a centrifugation tube, the centrifugation tube comprising a planar filter supported so as to divide the centrifugation tube into an upper space and a lower space and water-absorbing resin particles disposed on the filter, to bring the liquid sample into contact with the water-absorbing resin particles so that substantially all of a liquid phase part of the liquid sample is absorbed by the water-absorbing resin particles and the microorganism or the cell is caught on a surface of the water-absorbing resin particles;

pouring a collecting solution into the centrifugation tube to bring the collecting solution into contact with the water-absorbing resin particles, so as to collect the microorganism or the cell caught on the surface of the water-absorbing resin particles in the collecting solution; and

centrifuging the centrifugation tube so that the collecting solution containing the microorganism or the cell (i) separates from the water-absorbing resin particles by passing through the filter and (ii) accumulates at a bottom of the centrifugation tube,

wherein the collecting solution is poured into the centrifugation tube without separating the liquid phase part absorbed by the water-absorbing resin particles from the water-absorbing resin particles that have absorbed the liquid phase part.

2-3. (canceled)

4. (rejected) The method according to claim 1, wherein the centrifugation is performed at 500 to 13000 g for 3 seconds to 60 minutes.

5. (rejected) The method according to claim 1, wherein an amount of the liquid sample added is not greater than a water-absorbing capacity of the water-absorbing resin particles.

6. (rejected) The method according to claim 1, wherein an amount of the collecting solution added is greater than a water-absorbing capacity of the water-absorbing resin particles that have absorbed the liquid phase part

7. (rejected) The method according to claim 1, wherein the water-absorbing resin particles are a hydrophilic cross-linked polymer having a hydrophilic functional group.

8. (rejected) The method according to claim 1, wherein the microorganism to be collected is at least one selected from the group consisting of acid-fast bacteria, atypical mycobacteria, gonococcus, legionella bacteria, mycoplasmas, spirochetes, syphilis spirochetes, chlamydiae, rickettsiae, *Mycobacterium leprae*, Spirillum minus, staphylococci, streptococci, *Escherichia coli*, *Pseudomonas aeruginosa*, *Pasteurella pestis*, viruses, Japanese encephalitis virus, hepatitis B virus, hepatitis C virus, ATLV, HIV, and Ebola virus.

9. (rejected) The method according to claim 8, wherein the acid-fast bacterium is at least one selected from the group consisting of *M. avium*, *M. intracellularae*, *M. gordonae*, *M. tuberculosis*, *M. kansasii*, *M. fortuitum*, *M. chelonae*, *M. bovis*, *M. scrofulaceum*, *M. paratuberculosis*, *M. phlei*, *M. marinum*, *M. simiae*, *M. scrofulaceum*, *M. szulgai*, *M. leprae*, *M. xenopi*, *M. ulcerans*, *M. lepraemurium*, *M. flavescens*, *M. terrae*, *M. nonchromogenicum*, *M.*

malmoense, *M. asiaticum*, *M. vaccae*, *M. gastri*, *M. triviale*, *M. haemophilum*, *M. africanum*, *M. thermoresistable*, and *M. smegmatis*.

10. (rejected) The method according to claim 1, wherein the liquid sample is at least one selected from the group consisting of sputum, spinal fluid, feces, saliva, blood, tissues, swab, liquid obtained by gastrolavage, urine, samples obtained by pretreating these biological samples, water in baths, water in swimming pools, water in fish farms, water in rivers, lake water, and seawater.

11. (rejected) The method according to claim 1, wherein the amount of the liquid sample is in a range from 50 μL to 500 μL.

12. (rejected) The method according to claim 1, wherein the amount of the liquid sample is in a range from 50 mL to 200 mL.

13. (canceled)

14. (rejected) A method of amplifying or detecting specifically a gene of a microorganism or a cell, comprising:

collecting a microorganism or a cell by the method according to claim 1;

extracting a gene of the microorganism or the cell by adding an extraction reagent solution containing a nonionic detergent to the microorganism or the cell and heating a resultant mixture; and

amplifying or detecting specifically an extracted gene.

15. (rejected) The method according to claim 14, wherein the extraction reagent solution also serves as the collecting solution.

16. (rejected) The method according to claim 14, wherein a heating temperature is between 70°C and 100°C.

17. (rejected) The method according to claim14, wherein the heating is performed for 1 to 30 minutes.

18. (rejected) The method according to claim 14, wherein the heating is performed at 96°C for 10 minutes.

19. (rejected) The method according to claim 14, wherein a pH of the extraction reagent solution is in a range from 7.0 to 12.0.

20. (rejected) The method according to claim 14, wherein a concentration of the nonionic detergent in the extraction reagent solution is in a range from 0.01 to 10 wt%.

21. (rejected) The method according to claim 14, wherein the nonionic detergent is at least one selected from the group consisting of D-sorbitol fatty acid esters, polyoxyethyleneglycol sorbitan alkyl esters, and polyoxyethyleneglycol p-t-octylphenyl ethers.

22. (rejected) The method according to claim 14, wherein the extraction reagent solution further contains a metal chelating agent.

23. (rejected) The method according to claim 22, wherein a concentration of the metal chelating agent in the extraction reagent solution is 0.1 to 100 mM.

24. (rejected) The method according to claim 22, wherein the metal chelating agent is at least one selected from the group consisting of ethylenediaminetetraacetic acid (EDTA), ethylene glycol bis(β-aminoethyl ether)-N,N,N',N'-tetraacetic acid (EGTA), diaminocyclohexane tetraacetic acid, o-phenanthroline, and salicylic acid.

25. (rejected) The method according to claim 14, wherein the gene is amplified or detected specifically by a polymerase chain reaction (PCR) method.

26. (rejected) The method according to claim 1, wherein the filter is made of at least one selected from the group consisting of polyvinylidene fluoride, cellulose nitrate, hydrophilic polyethersulfone, polytetrafluoroethylene, polycarbonate, polyamide, polysulfone, polyethylene, polypropylene and acetylcellulose.

APPENDIX B - EVIDENCE

Not applicable

APPENDIX C - RELATED PROCEEDINGS

Not applicable